AUSTRALIAN PRODUCT INFORMATION

ENDONE®

(oxycodone hydrochloride) tablets

WARNINGS

Limitations of Use

Because of the risks associated with the use of opioids, ENDONE should only be used in patients for whom other treatment options, including non-opioid analgesics, are ineffective, not tolerated or otherwise inadequate to provide appropriate management of pain (see Section 4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Hazardous and Harmful Use

ENDONE poses risks of hazardous and harmful use which can lead to overdose and death. Assess the patient's risk of hazardous and harmful use before prescribing and monitor the patient regularly during treatment (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Life Threatening Respiratory Depression

Serious, life-threatening or fatal respiratory depression may occur with the use of ENDONE. Be aware of situations which increase the risk of respiratory depression, modify dosing in patients at risk and monitor patients closely, especially on initiation or following a dose increase (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Concomitant Use of Benzodiazepines and Other Central Nervous System (CNS) Depressants, including alcohol

Concomitant use of opioids with benzodiazepines, gabapentinoids, antihistamines, tricyclic antidepressants, antipsychotics, cannabis or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma and death. Limit dosages and durations to the minimum required; and monitor patients for signs and symptoms of respiratory depression and sedation. Caution patients not to drink alcohol while taking ENDONE.

1 NAME OF THE MEDICINE

Oxycodone hydrochloride

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ENDONE tablet contains 5 mg of oxycodone hydrochloride as the active ingredient.

Excipients of known effect: sugars as lactose.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

ENDONE tablets are a white, round, biconvex 10 mm tablet with one side embossed "O 5" with a break bar on the other side.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

ENDONE is indicated for the short-term management of severe pain for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain.

4.2 DOSE AND METHOD OF ADMINISTRATION

Usual Adult Dose

5 mg every six hours, preferably after meals or with milk. Do not divide the tablet.

It may be necessary to increase the usual dose in cases of more severe pain or in those who have become tolerant of narcotics.

In patients with hepatic and renal impairment, dosage should be reduced and adjusted according to the clinical situation (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

4.3 CONTRAINDICATIONS

Hypersensitivity to opiate narcotics, cor pulmonale, cardiac arrhythmias, bronchial asthma, acute alcoholism, brain tumour, head injuries, increased cerebrospinal or intracranial pressure, severe CNS depression, severe respiratory disease, acute respiratory disease and respiratory depression, convulsive disorders, delirium tremens, suspected surgical abdomen and concomitant MAOIs or within 14 days of such therapy.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Hazardous and Harmful Use

ENDONE contains the opioid oxycodone and is a potential drug of abuse, misuse and addiction. Addiction can occur in patients appropriately prescribed ENDONE at recommended doses.

The risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or mental illness. The risk also increases the longer the drug is used and with higher doses. Patients should be assessed for their risks for opioid abuse or addiction prior to being prescribed ENDONE.

All patients receiving opioids should be routinely monitored for signs of misuse and abuse. Opioids are sought by people with addiction and may be subject to diversion. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the safe storage and proper disposal of any unused drugs (see Sections 6.4 SPECIAL PRECAUTIONS FOR STORAGE and 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL). Caution patients that abuse of oral or transdermal forms of opioids by parenteral administration can result in serious adverse events, which may be fatal.

Patients should be advised not to share ENDONE with anyone else.

Respiratory Depression

Serious, life-threatening or fatal respiratory depression can occur with the use of opioids even when used as recommended. It can occur at any time during the use of ENDONE, but the risk is greatest during initiation of therapy or following an increase in dose. Patients should be monitored closely for respiratory depression at these times.

The risk of life-threatening respiratory depression is also higher in elderly, frail or debilitated patients; in patients with existing impairment of respiratory function (e.g. chronic obstructive pulmonary disease; asthma) and in patients with hepatic and renal impairment (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE – Use in Hepatic and Renal Impairment). Opioids should be used with caution and with close monitoring in these patients (see Section 4.2 DOSE AND METHOD OF

ADMINISTRATION). The use of opioids is contraindicated in patients with severe respiratory disease, acute respiratory disease and respiratory depression (see Section 4.3 CONTRAINDICATIONS).

The risk of respiratory depression is greater with the use of high doses of opioids, especially high potency and modified release formulations, and in opioid-naïve patients. Initiation of opioid treatment should be at the lower end of the dosage recommendations with careful titration of doses to achieve effective pain relief. Careful calculation of equianalgesic doses is required when changing opioids or switching from immediate-release to modified-release formulations, together with consideration of pharmacological differences between opioids. Consider starting the new opioid at a reduced dose to account for individual variation in response.

Sleep-related Breathing Disorders

Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage.

Adrenal Insufficiency

Adrenal insufficiency has been reported with opioid use, more often following long-term use. Symptoms may include nausea, vomiting, anorexia, fatigue, weakness, dizziness, or low blood pressure. If adrenal insufficiency is suspected, appropriate laboratory testing is recommended and discontinuation of treatment with ENDONE should be considered.

Endocrine Effects

Opioids, such as ENDONE, may influence the hypothalamic-pituitary-adrenal or –gonadal axes. Hormonal disturbances that have been observed include an increase in serum prolactin and decreases in plasma cortisol and testosterone. Clinical symptoms may manifest from these hormonal changes.

Androgen deficiency may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility.

Neonatal Withdrawal Syndrome

Chronic use of oxycodone by the mother at the end of pregnancy may result in a withdrawal syndrome (e.g. hypertonia, neonatal tremor, neonatal agitation, myoclonus, convulsions, apnoea or bradycardia) in the neonate. In many reported cases the withdrawal was serious and required treatment. The syndrome is generally delayed for several hours to several days after birth. (See Section 4.6 FERTILITY, PREGNANCY AND LACTATION - Use in Pregnancy).

Gastrointestinal Toxicity

Reports of significant oesophageal dysfunction have been observed via high-resolution manometry in patients taking opioid medicines on a long-term basis. Discontinuation or weaning of opioids should be considered in patients presenting with oesophageal complaints including but not limited to dysphagia, regurgitation, or non-cardiac chest pain.

Risks from Concomitant Use of Benzodiazepines or Other CNS Depressants, including alcohol

Concomitant use of opioids and benzodiazepines or other CNS depressants, including alcohol, may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of ENDONE with CNS depressant medicines, such as other opioid analgesics, benzodiazepines, gabapentinoids, cannabis, sedatives, hypnotics, tricyclic antidepressants, antipsychotics, antihistamines, centrally-active anti-emetics and other CNS depressants, should be reserved for patients for whom other treatment options are not possible. If a decision is made to prescribe ENDONE concomitantly with any of the medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible. Patients should be followed closely for signs and symptoms of respiratory depression and sedation. Patients and their caregivers should be made aware of these symptoms. Patients and their caregivers should also be informed of the potential harms of consuming alcohol whilst taking ENDONE.

Use of Opioids in Chronic (long-term) Non-cancer Pain (CNCP)

Opioid analgesics have an established role in the treatment of acute pain, cancer pain and palliative and end-of-life care. Current evidence does not generally support opioid analgesics in improving pain and function for most patients with CNCP. The development of tolerance and physical dependence and risks of adverse effects, including hazardous and harmful use, increase with the length of time a patient takes an opioid. The use of opioids for long-term treatment of CNCP is not recommended.

The use of an opioid to treat CNCP should only be considered after maximised non-pharmacological and non-opioid treatments have been tried and found ineffective, not tolerated or otherwise inadequate to provide sufficient management of pain. Opioids should only be prescribed as a component of comprehensive multidisciplinary and multimodal pain management.

Opioid therapy for CNCP should be initiated as a trial in accordance with clinical guidelines and after a comprehensive biopsychosocial assessment has established a cause for the pain and the appropriateness of opioid therapy for the patient (see Hazardous and Harmful Use above). The expected outcome of therapy (pain reduction rather than complete abolition of pain, improved function and quality of life) should be discussed with the patient before commencing opioid treatment, with agreement to discontinue treatment if these objectives are not met.

Owing to the varied response to opioids between individuals, it is recommended that all patients be started at the lowest appropriate dose and titrated to achieve an adequate level of analgesia and functional improvement with minimum adverse reactions. Immediate-release products should not be used to treat chronic pain but may be used for a short period in opioid-naïve patients to develop a level of tolerance before switching to a modified-release formulation. Careful and regular assessment and monitoring is required to establish the clinical need for ongoing treatment. Discontinue opioid therapy if there is no improvement of pain and/or function during the trial period or if there is any evidence of misuse or abuse. Treatment should only continue if the trial has demonstrated that the pain is opioid responsive and there has been functional improvement. The patient's condition should be reviewed regularly, and the dose tapered off slowly if opioid treatment is no longer appropriate (see Ceasing Opioids).

Tolerance, Dependence and Withdrawal

Neuroadaptation of the opioid receptors to repeated administration of opioids can produce tolerance and physical dependence. Tolerance is the need for increasing doses to maintain analgesia. Tolerance may occur to both the desired and undesired effects of the opioid.

Physical dependence, which can occur after several days to weeks of continued opioid usage, results in withdrawal symptoms if the opioid is ceased abruptly or the dose is significantly reduced. Withdrawal symptoms can also occur following the administration of an opioid antagonist (e.g. naloxone) or partial agonist (e.g. buprenorphine). Withdrawal can result in some or all of the following symptoms: dysphoria, restlessness/agitation, lacrimation, rhinorrhoea, yawning, sweating, chills, myalgia, mydriasis, irritability, anxiety, increasing pain, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhoea, increased blood pressure, increased respiratory rate and increased heart rate.

When discontinuing ENDONE in a person who may be physically-dependent, the drug should not be ceased abruptly but withdrawn by tapering the dose gradually (see Ceasing Opioids below and Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Accidental Ingestion/Exposure

Accidental ingestion or exposure of ENDONE, especially by children, can result in a fatal overdose of oxycodone. Patients and their caregivers should be given information on safe storage and disposal of unused ENDONE (see Sections 6.4 SPECIAL PRECAUTIONS FOR STORAGE and 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL).

Hyperalgesia

Hyperalgesia may occur with the use of opioids, particularly at high doses. Hyperalgesia may manifest as an unexplained increase in pain, increased levels of pain with increasing opioid dosages or diffuse sensitivity not associated with the original pain. Hyperalgesia should not be confused with tolerance (see Tolerance, Dependence and Withdrawal above). If opioid induced hyperalgesia is suspected, the dose should be reduced and tapered off if possible. A change to a different opioid may be required.

Ceasing Opioids

Abrupt discontinuation or rapid decreasing of the dose in a person physically dependent on an opioid may result in serious withdrawal symptoms and uncontrolled pain (see Tolerance, Dependence and Withdrawal above). Such symptoms may lead the patient to seek other sources of licit or illicit opioids. Opioids should not be ceased abruptly in a patient who is physically dependent but withdrawn by tapering the dose slowly. Factors to take into account when deciding how to discontinue or decrease therapy include the dose and duration of the opioid the patient has been taking, the type of pain being treated and the physical and psychological attributes of the patient. A multimodal approach to pain management should be in place before initiating an opioid analgesic taper. During tapering, patients require regular review and support to manage any increase in pain, psychological distress and withdrawal symptoms.

There are no standard tapering schedules suitable for all patients and an individualised plan is necessary. In general, tapering should involve a dose reduction of no more than 10 to 25% every 2 to 4 weeks (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION). If the patient is experiencing increased pain or serious withdrawal symptoms, it may be necessary to go back to the previous dose until stable before proceeding with a more gradual taper.

When ceasing opioids in a patient who has a suspected opioid use disorder, the need for medication assisted treatment and/or referral to a specialist should be considered.

Other Information

Oxycodone should be used with extreme caution in patients with head injuries and raised intracranial pressure as respiratory depression and ability to increase CSF pressure may be exaggerated, thereby complicating the clinical course.

Administration of oxycodone may result in severe hypotension in patients whose ability to maintain adequate blood pressure is compromised by reduced blood volume, or concurrent administration of such drugs as phenothiazines or certain anaesthetics. Oxycodone may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Opioid analgesics should be used with caution in patients with myasthenia gravis.

The euphoric activity of opioid compounds has led to their abuse. It should be given with caution or in reduced doses to patients with hypothyroidism, adrenocortical insufficiency, impaired kidney or liver function, prostatic hypertrophy or shock. It should be used with caution in patients with obstructive bowel disorders.

Use in Hepatic and Renal Impairment

The plasma concentration of oxycodone may be increased in patients with hepatic or renal impairment. Therefore, dosage in such patients should be reduced and adjusted according to the clinical situation.

Use in the Elderly

Oxycodone should be administered with caution, and in reduced dosages, to elderly or debilitated patients.

Paediatric Use

Oxycodone should not be administered to children.

Effects on Laboratory Tests

No data available.

Hepatobiliary Disorders

Oxycodone may cause dysfunction and spasm of the sphincter of Oddi, thus increasing the risk of biliary tract symptoms and pancreatitis. Therefore, oxycodone has to be administered with caution in patients with pancreatitis and diseases of the biliary tract.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Generally, the effects of oxycodone may be antagonised by acidifying agents and potentiated by alkalising agents.

Concurrent administration of oxycodone with anticholinergic agents may result in an increased risk of severe constipation and/or urinary retention.

Oxycodone may potentiate hypotensive effects when used concurrently with antihypertensive agents, especially ganglionic blockers, leading to increased risk of orthostatic hypotension.

Concurrent use of oxycodone with hydroxyzine or alcohol and CNS depressants (including other opioid agonist analgesics, sedative hypnotics, general anaesthetics, phenothiazines, tricyclic antidepressants, antihistamines, centrally-active anti-emetics, gabapentinoids and cannabis) may result in increased CNS depressant, respiratory depressant and hypotensive effects. Caution is recommended and the dosage of one or both agents should be reduced (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE – Risks from Concomitant Use of Benzodiazepines or Other CNS Depressants, including alcohol).

Mixed agonist/antagonist analgesics (including pentazocine, butorphanol, buprenorphine) may reduce the analgesic effect of oxycodone and/or may precipitate withdrawal symptoms. Naloxone and naltrexone antagonise the analgesic, CNS and respiratory depressant effects of oxycodone and precipitate withdrawal symptoms. Dosage of the antagonist agents should be carefully titrated when used to treat opioid overdosage in dependent patients.

Concurrent administration of oxycodone with serotonin agents, such as a Selective Serotonin Reuptake Inhibitor (SSRI) or a Serotonin Noradrenaline (Norepinephrine) Reuptake Inhibitor (SNRI) may cause serotonin toxicity. The symptoms of serotonin toxicity may include mental-status changes (e.g. agitation, hallucinations, coma), autonomic instability (e.g. tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g. hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea). Oxycodone should be used with caution and the dosage may need to be reduced in patients using these medications.

Oxycodone hydrochloride is metabolised in the intestine and liver to form noroxycodone and oxymorphone via cytochrome P450 isoenzymes of the CYP3A4 and CYP2D6, respectively. Metabolic interactions with drugs that involve the cytochrome P450 enzyme system (CYP3A4, CYP2D6) can cause the plasma concentration of oxycodone to increase. Quinidine, which is a potent CYP2D6 inhibitor, has blocked the formation of oxymorphone, while the oxycodone concentration increased marginally. Concurrent administration of quinidine does not alter the pharmacodynamic effects of oxycodone. The metabolic pathway may be blocked by various drugs (e.g. cimetidine, certain cardiovascular drugs and antidepressants), although such blockade has not yet been shown to be of clinical significance with oxycodone. The potential effects of oxycodone on CYP enzymes have not been studies either *in vitro* or *in vivo*.

Oxycodone may antagonise the effects of metoclopramide on gastrointestinal motility.

Oxycodone may enhance the effects of neuromuscular blocking agents resulting in increased respiratory depression.

Nonselective MAOIs (including furazolidone, pargyline and procarbazine) intensify the effects of oxycodone which can cause anxiety, confusion and significant respiratory depression. Oxycodone should not be given to patients taking nonselective MAOIs or within 14 days of stopping such treatment. As it is unknown whether there is an interaction between selective MAOIs (e.g. selegiline) and oxycodone, caution is advised with this drug combination.

Oxycodone may increase the anticoagulant activity of coumarin derivatives.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

Studies have not been performed to assess the effects of oxycodone on fertility.

Use in Pregnancy

Pregnancy category: C

Reproductive toxicity studies with oxycodone in animals have not been conducted. Opioid analgesics cross the placenta. The use of oxycodone during labour may cause respiratory depression in the newborn infant. Neonatal withdrawal syndrome has been reported in newborn infants with chronic maternal use of oxycodone during pregnancy. Babies born to opioid-dependent mothers may be physically dependent and suffer withdrawal symptoms (convulsions, irritability, excessive crying, tremors, hyperactive reflexes, fever, vomiting, diarrhoea, sneezing and yawning).

Use in Lactation

Reproductive toxicity studies with oxycodone in animals have not been conducted. Oxycodone is excreted into human milk in low concentrations. Because of the possibility of adverse effects in breastfed infants (sedation, respiratory depression, withdrawal symptoms upon cessation of maternal administration), oxycodone is not recommended for breastfeeding mothers unless the expected benefits outweigh the potential risk.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Oxycodone may impair the mental and/or physical abilities needed for certain potentially hazardous activities, such as driving a car or operating machinery. Patients should be cautioned accordingly.

This medication may cause drowsiness. Avoid alcohol.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Adverse drug reactions are typical of full opioid agonists; tolerance (except constipation) generally develops with long term use. In normal doses, the most common side effects of oxycodone are nausea, vomiting, constipation, drowsiness, unusual tiredness or weakness, vertigo, faintness, light-headedness, orthostatic hypotension and confusion. Less frequent side effects include dry mouth, sweating, facial flushing, nervousness or restlessness. Micturition may be difficult and there may be ureteric or biliary spasm; there is also an anti-diuretic effect. Raised intracranial pressure occurs in some patients. Other uncommon side effects such as bradycardia, supraventricular tachycardia, palpitations, anorexia, changes of mood, respiratory depression, hallucinations have been reported; CNS stimulation, paradoxical and convulsions may occur especially in children. Due to the histamine-releasing effect, allergic reactions such as urticaria and pruritus occur in some individuals. Muscle rigidity has been reported following high doses. Larger doses produce respiratory depression and hypotension, with circulatory failure and deepening coma. Convulsions may occur in infants and children. Death may occur from respiratory failure. Side effects with an unknown frequency include sphincter of Oddi dysfunction, central sleep apnoea syndrome, pancreatitis, adrenal insufficiency and androgen deficiency.

In long term use, physical and psychological dependence and tolerance may develop.

The following withdrawal symptoms may be observed after narcotics are discontinued: body aches, diarrhoea, gooseflesh, loss of appetite, nervousness, restlessness, runny nose, sneezing, tremors or shivering, stomach cramps, nausea, trouble with sleeping, unusual increase in sweating and yawning, weakness, tachycardia and unexplained fever. With appropriate medical use of narcotics and gradual withdrawal from the drug, these symptoms are usually mild.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Symptoms

Toxic doses of opioids vary considerably with the individual and regular users may tolerate large doses. Serious overdosage with oxycodone is characterised by respiratory depression and somnolence progressing to coma and skeletal muscle flaccidity. Toxic leukoencephalopathy has been observed with oxycodone overdose. Hypoglycaemia, cardiac arrest and death may occur. Rhabdomyolysis progressing to renal failure has been reported in opioid overdosage. Pulmonary oedema after overdosage is a common cause of fatalities among opiate addicts.

Treatment

Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including oxycodone. Therefore, an appropriate dose of naloxone (usual adult dose: 0.4 mg) should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

Oxygen, intravenous fluids, vasopressors and other supportive measures should be used as indicated. Activated charcoal may be given by mouth in conscious patients if an overdose has been ingested within 1 hour or so.

In an individual physically dependent on narcotics, the administration of the usual dose of a narcotic antagonist will precipitate an acute withdrawal syndrome. The severity of this syndrome will depend on the degree of physical dependence and the dose of antagonist administered. The use of narcotic antagonists in such individuals should be avoided if possible. If a narcotic antagonist must be used to treat serious respiratory depression in the physically dependent patient, only 10 to 20% of the usual initial dose of the antagonist should be administered.

In severe toxicity, the cardiovascular system is usually depressed and requires supportive treatment. If hypotension is due to vasodilatation, plasma expansion, or even vasopressors may be required. Additional measures include support of electrolyte balance, maintenance of normal temperature, catheterisation of the bladder to avoid distension and symptomatic treatment of itching, nausea, vomiting, headache and confusion during the recovery period.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Oxycodone, the principal ingredient, is 14-hydroxydihydrocodeinone, which is derived from the opium alkaloid, thebaine. It is a semisynthetic narcotic analgesic with multiple actions qualitatively similar to those of morphine. Oxycodone is an opioid agonist and binds to μ– (mu) and more weakly to κ– (kappa) and δ– (delta) opioid receptor subtypes. Opioid receptor binding by oxycodone in the central nervous system produces analgesia with some associated sedation. Additional pharmacologically mediated effects of oxycodone involve the CNS, smooth muscle and cardiovascular system.

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Oxycodone is absorbed from the gastrointestinal tract.

Distribution

Following oral administration of ENDONE, the analgesic effect occurs within 10 to 15 minutes, reaches its maximum in 30 to 60 minutes, and persists for 3 to 6 hours (nontolerant patients only; duration decreases as tolerance develops during chronic therapy).

Metabolism

It is extensively metabolised to noroxycodone via cytochrome P450 isoenzymes of the CYP3A family and, to a lesser extent, to oxymorphone via CYP2D6.

Excretion

Oxycodone metabolites undergo glucuronidation and are excreted with unchanged drug in urine. The elimination half-life is reported to be 2 to 4 hours.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Oxycodone was not mutagenic in the Ames *Salmonella and Escherichia coli* assays; but was positive in the mouse lymphoma assay. In assays of chromosomal damage, genotoxic effects occurred in the human lymphocyte chromosomal aberration assay *in vitro*, but not in the *in vivo* bone marrow micronucleus assay in mice.

Carcinogenicity

Studies of oxycodone in animals to evaluate its carcinogenic potential have not been conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

ENDONE tablets also contain stearic acid, microcrystalline cellulose and lactose.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Container type: blister pack (PVC/PVDC/Al)

Pack size: 6, 8, 10, 20 and 500

Some pack sizes may not be marketed.

Australian Register of Therapeutic Goods (ARTG)

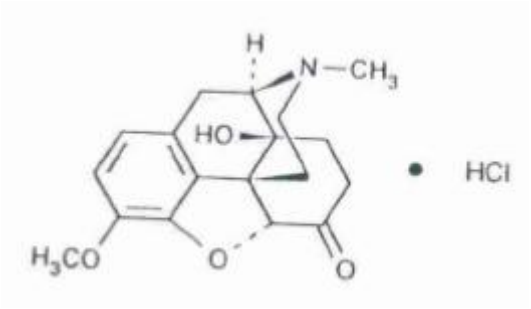
AUST R 14945 – ENDONE oxycodone hydrochloride 5 mg tablet blister pack

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical Structure



Oxycodone hydrochloride occurs as white to off-white, odourless, crystals or powder.

Oxycodone 1 g dissolves in 10 mL water. It is sparingly soluble in alcohol and nearly insoluble in ether.

Chemical name: 4,5α-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride

Molecular formula: $C_{18}H_{21}NO_4.HCl$

Molecular weight: 351.9

CAS Number

124-90-3

7 MEDICINE SCHEDULE (POISONS STANDARD)

S8 (Controlled Drug)

8 SPONSOR

Viatris Pty Ltd

Level 1, 30 The Bond

30 – 34 Hickson Road

Millers Point NSW 2000

www.viatris.com.au

Phone: 1800 274 276

9 DATE OF FIRST APPROVAL

9/09/1991

10 DATE OF REVISION

29/10/2026

Summary Table of Changes

Section Changed	Summary of New Information
4.5	Addition of drug interaction with SSRI or SNRI causing serotonin toxicity

ENDONE® is a Viatris company trade mark

ENDONE_pi\Nov26/00